



## Laws hinder drug development inspired by Amazonian biodiversity

SÃO PAULO — For her graduate work, Eliana Rodrigues spent several years splitting her time between two indigenous communities in the north of Brazil, studying their ritual healing practices and chronicling which plants they used for treatments. In a comprehensive survey of their practices, she identified 169 plant species used in 345 formulations to treat 68 different diseases (*J. Psychoactive Drugs* 38, 285–295, 2006). After detailing her initial findings, Rodrigues, now a professor at the Federal University of São Paulo, hoped to take some of the natural compounds found in these plants and turn them into commercial drug products, but legal hurdles paralyzed her work.

In 2001, after a scandal involving the Swiss drug giant Novartis and a consortium of British researchers who hoped to patent new compounds derived from microbes found in the Amazon, the Brazilian government imposed a tough law called Provisional Measure 2186. The legislation required drug companies and universities to pay indigenous communities a part of any profits stemming from traditional knowledge. Although it was aimed at protecting the exploitation of native biodiversity, critics say the law has severely limited scientists' access to the country's biological resources—even for basic research—and has hindered the development of medicines derived from natural products.

"The current legal framework is completely inadequate to a country that is said to value innovation," says Maria Celeste Emerick, science and technology management coordinator at the Oswaldo Cruz Foundation in Rio de Janeiro. "It doesn't suit the interest of university researchers, local pharmaceutical companies and traditional communities."

Because of the provisional measure—which, despite its name, was made permanent within a month of its initial passage—"companies have now become unmotivated," says João Batista Calixto, a pharmacologist at the Federal University of Santa Catarina in Florianópolis.

Calixto describes the challenges he himself has faced in regards to two natural compounds developed in his lab. One is an ointment for muscular pain made from the leaves of a shrub used by fishermen along the southeastern coast of Brazil; the other is an antiaging cream based on antiinflammatory substances found in a type of passion fruit. Both compounds were successfully commercialized and marketed more than four years ago. But last year, the Council for Genetic Heritage Management (CGEN), a federal administrative body created by the Environment Ministry to apply the



**Passion play:** The government cracked down on a cream derived from the *Passiflora* passion fruit.

provisional measure, fined both products' manufacturers for not having the necessary authorizations to deal with the plants. This year, around 100 more companies and universities have similarly been penalized for collecting plants or other organisms without authorization, leading some firms to suspend all projects involving biodiversity until the legal framework is made more business friendly.

At a meeting here in August, academics, drug company representatives and government officials met to discuss ways of simplifying access to genetic resources and easing legal provisions. "There is political will to make corrections in the provisional measure," CGEN President Braulio Dias told delegates of the meeting. "But to get congressional approval will not be easy."

### Navigating the labyrinth

Brazilian lawmakers have tacked dozens of resolutions and amendments onto the provisional measure since its initial passage ten years ago. The result has been a labyrinth of rules that have slowed down scientific progress and weakened the interaction between universities and pharmaceutical companies, experts say. To make matters worse, scientists hoping to cement intellectual property also have to abide by Law 9279—the 1996 legislation that prohibits the patenting of living organisms. According to Calixto, the double whammy of Law 9279 and Provisional Measure 2186 has sidelined development of drugs based on natural compounds and rendered the field of ethnopharmacology into academic obsolescence. The bureaucracy is so demanding, in fact, that many scientists prefer to work solely with synthetic compounds.

Against these odds, a handful of researchers have found ways of working within the system.

"The provisional measure is absurd but feasible," says Luis Carlos Marques, a pharmacist at Bandeirantes University in São Paulo. In 2008, as director of São Paulo-based Apsen Pharmaceuticals, he helped develop a bed sore medicine originating from a small tree with large, circular bean pods native to Brazil, called *barbatimão*. And, by working with the regulatory authorities, Marques managed to get CGEN approval to market the new product within ten months of filing an application.

Other Brazilian scientists still look to the natural world but try to find organisms that exist beyond the local ecosystem to skirt legal challenges. For instance, Farmabrazilis, a São Paulo-based nonprofit research network modeled after international development organizations such as OneWorld Health and the Global Alliance for TB Drug Development, is advancing two natural compounds—an immunomodulatory agent called P-MAPA that is produced by fungal fermentation and an antibiotic called violacein extracted from a particular bacterium. Neither of the organisms used to make these products are unique to Brazil and, so, are not protected by the provisional measure. "The current legal framework has not affected our research lines, because we don't work on material from Brazilian biodiversity," says Farmabrazilis chief executive Iseu Nunes.

As for Rodrigues, she has opted to work within the system and secure all the necessary paperwork to continue the anthropological and botanical research she started more than ten years ago. She and her team are now studying the antianxiety effects of a native herb used in religious rituals and the painkilling effects of an Amazonian frog secretion on headaches. "Now I have all the bureaucratic authorizations required to do my work," Rodrigues says.

*Carlos Henrique Fioravanti*